mixed solvent of ethyl acetate and n-hexane, 4-chloro-4'-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]benzanilide (105 mg) was obtained as colorless powder crystals.

Example 3

A mixture of 4'-chloro-5-(4-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)thiophene-2-carboxyanilide (360 mg), methyl iodide (199 mg), potassium carbonate (129 mg) and DMF (5 ml) was stirred at room temperature for 3 days. Water (10 ml) was added to the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 9:1 - 4:1) and then recrystallized from a mixed solvent of ethyl acetate and n-hexane to give 4'-chloro-5-(1,4-dimethyl-5-trifluoromethyl-1H-pyrazol-3-yl)thiophene-2-carboxyanilide (13 mg) as colorless powder crystals.

Example 4

In the silica gel column chromatography treatment of Example 3, a compound eluted after the compound of Example 3 was recrystallized from a mixed solvent of ethyl acetate and hexane to give 4'-chloro-5-(1,4-dimethyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carboxyanilide (86 mg) as colorless powder crystals.

Example 5

A mixture of 5-(1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carbonyl chloride (150 mg) and dichloromethane (1.5 ml) was added under ice-cooling to a mixture of 2-chloroaniline (68 mg), pyridine (42 mg) and dichloromethane (2 ml), followed by stirring for 30 minutes at room temperature. Saturated sodium hydrogencarbonate aqueous solution was added to the reaction mixture, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The resulting organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was recrystallized from ethanol to give 2'-chloro-5-(1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carboxyanilide (80 mg) as colorless crystals.

Example 6

5-(1-Methyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carbonyl chloride (295 mg) and THF (3 ml) were added to a mixture of 2-amino-1-methylpyrrole hydrochloride (202 mg), potassium carbonate (553 mg), THF (2 ml) and water (4 ml), followed by stirring at room temperature for 30 minutes. Water was added to the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with 1 N hydrochloric acid, saturated sodium bicarbonate

aqueous solution and water in that order. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 2:1 - 3:2) and then recrystallized from a mixed solvent of ethyl acetate and n-hexane to give N-(1-methyl-2-pyrrolyl)-5-(1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carboxamide (126 mg) as light yellow powder crystals.

Example 7

5-(1-Methyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carbonyl chloride (150 mg) and THF (2 ml) were added to a mixture of 70% ethylamine aqueous solution (1 ml) and THF (2 ml), followed by stirring at room temperature for 2 hours. Water was added to the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was recrystallized from a mixed solvent of ethyl acetate and n-hexane to give N-ethyl-5-(1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carboxamide (96 mg) as colorless powder crystals.

Example 8

5-(1-Methyl-5-trifluoromethyl-1H-pyrazol-3-yl)thiophene-2-carbonyl chloride (100 mg) and dichloromethane (2 ml) were added to a mixture of 2-aminothiazole (68 mg), saturated sodium bicarbonate aqueous solution (1 ml) and dichloromethane (1 ml), followed by stirring at room temperature for 5 hours. Water was added to the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 4:1 - 2:1) and then washed with diethyl ether to give 5-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)-N-(2-thiazolyl)thiophene-2-carboxamide (68 mg) as colorless solid.

Example 9

Sodium methoxide (257 mg) was added to a mixture of 3'-acetyl-4-chlorobenzanilide (1.00 g) and methanol (10 ml) under ice-cooling, followed by stirring at room temperature for 2 hours. Ethyl trifluoroacetate (0.522 ml) was added to the reaction solution under ice-cooling, followed by stirring under heat reflux for 3 days. Water (50 ml) was added to the reaction mixture, the thus formed product was extracted with ethyl acetate and then the

extract was washed with saturated brine. The organic layer was dried over anhydrous sodium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 2:1 - 1:1) to give a light yellow oil. A mixture of this oil with methyl hydrazine (0.122 ml), acetic acid (1 ml) and ethanol (10 ml) was stirred under heat reflux for 15 hours. After spontaneous cooling, the reaction solution was concentrated under a reduced pressure. After adding ethyl acetate, the thus obtained residue was washed with saturated sodium bicarbonate aqueous solution and saturated brine in that order. The organic layer was dried over anhydrous sodium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 6:1) and then recrystallized from a mixed solvent of ethyl acetate and n-hexane to give 4-chloro-3'-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)benzanilide (60 mg) as colorless powder crystals.

Example 10

In the silica gel column chromatography treatment of Example 9, a compound eluted after the compound of Example 9 was recrystallized from a mixed solvent of ethyl acetate and hexane to give 4-chloro-3'-(1-methyl-3-

trifluoromethyl-1H-pyrazol-5-yl)benzanilide (134 mg) as colorless powder crystals.

Example 11

Sodium triacetoxyborohydride (530 mg) was added to a mixture of 5-(1-methyl-5-trifluoromethyl-1H-pyrazol-3-yl)thiophene-2-carboxy aldehyde (260 mg), 4-chloroaniline (134 mg), acetic acid (0.1 ml) and dichloromethane (3 ml), followed by stirring at room temperature for 2 hours and 20 minutes. Saturated sodium bicarbonate aqueous solution (10 ml) was added to the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 10:1 - 6:1) to give 3-[5-[(4-chloroanilino)methyl]-2-thienyl]-1-methyl-5-trifluoromethyl-1H-pyrazole (313 mg) as a colorless solid.

Example 12

A mixture of ethyl 1-[4-(4-chlorobenzoylamino)phenyl]-5-trifluoromethyl-1H-pyrazole-4-carboxylate (150 mg), 1 N sodium hydroxide aqueous solution (1 ml) and ethanol (2 ml) was stirred at 45°C for 4 hours. After spontaneous cooling, 1 N hydrochloric acid aqueous solution (2 ml) was added to the reaction solution, the thus formed product was extracted

with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was recrystallized from ethanol to give 1-[4-(4-chlorobenzoylamino)phenyl]-5-trifluoromethyl-1H-pyrazole-4-carboxylic acid (91 mg) as colorless powder crystals.

Example 13

A mixture of 1-tert-butoxycarbonylpiperidine-4-carboxylic acid (198 mg), 4-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)aniline (206 mg), WSCD hydrochloride (172 mg) and THF (3 ml) was stirred overnight at room temperature. After adding ethyl acetate, the reaction solution was washed with water, saturated sodium bicarbonate aqueous solution, 1 N hydrochloric acid and saturated brine in that order. The organic layer was dried over anhydrous sodium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 7:1 - 5:1) to give tert-butyl 4-[4-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]phenylaminocarbonyl]piperidine-1-carboxylate (279 mg) as a colorless amorphous solid. 4 N Hydrochloric acid ethyl acetate solution (2.60 ml) was added to a mixture of this solid (263 mg) and ethyl acetate (2.6 ml), followed by stirring at room temperature for 2 hours and 45

minutes. The reaction solution was concentrated under a reduced pressure, diethyl ether was added to the thus obtained residue, and the mixture was concentrated under a reduced pressure. By recrystallizing the resulting residue from a mixed solvent of ethyl acetate and n-hexane, [4'-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]piperidine-4-carboxyanilide hydrochloride (201 mg) was obtained as colorless powder crystals.

Example 14

Methanesulfonyl chloride (80 mg) was added to a mixture of ethyl 1-(4-aminophenyl)-5-trifluoromethyl-1H-pyrazole-4-carboxylate (150 mg), triethylamine (76 mg) and THF (2 ml) under ice-cooling, followed by stirring at room temperature for 4 hours. Thereafter, the same treatment of Example 2 was carried out to give ethyl 1-(4-methanesulfonylaminophenyl)-5-trifluoromethyl-1H-pyrazole-4-carboxylate (29 mg) as a colorless solid.

Example 15

To a mixture of 5-(1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl)thiophene-2-carboxy aldehyde (583 mg), diethyl 4-chloro-α-fluorobenzylphosphonate (755 mg) and THF (8 ml) was added at -60°C lithium diisopropylamide prepared from diisopropylamine (259 mg) and an n-butyl lithium-n-hexane solution (1.6 N, 1.6 ml), followed by stirring for 6 hours and 30 minutes while gradually warming it to room temperature. Water (10 ml) was added to

the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 16:1 - 8:1) to give 5-[5-[(E)-2-(4-chlorophenyl)-2-fluorovinyl]-2-thienyl]-1-methyl-3-trifluoromethyl-1H-pyrazole (32 mg) as an yellow oil.

Example 16

4-Chlorophenyl isocyanate (461 mg) was added to a mixture of 4-(1-methyl-3-trifluoromethyl-1H-pyrazol-5-yl)piperidine (540 mg) and THF (5 ml) under ice-cooling, followed by stirring overnight at room temperature. Water (10 ml) was added to the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. A mixed solvent of acetone and diethyl ether was added to the thus obtained residue, the insoluble matter was removed by filtration and then the filtrate was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 1:1) and then recrystallized from a mixed solvent of ethyl acetate and n-hexane to give 4'-chloro-4-(1-methyl-3-

trifluoromethyl-1H-pyrazol-5-yl)piperidine-1-carboxyanilide (391 mg) as colorless powder crystals.

Example 17

A mixture of 1-trityl-1H-imidazole-4-carboxylic acid (300 mg), 4-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl)aniline (200 mg), WSCD hydrochloride (162 mg), DMF (0.5 ml) and THF (4 ml) was stirred overnight at room temperature. Water (10 ml) was added to the reaction solution, the thus formed product was extracted with ethyl acetate and then the extract was washed with saturated brine. The organic layer was dried over anhydrous magnesium sulfate and then concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 3:1). Then, concentrated hydrochloric acid (0.1 ml) and acetone (3 ml) were added, followed by stirring overnight at room temperature. The reaction solution was concentrated under a reduced pressure, diethyl ether was added to the thus obtained residue, and then the mixture was concentrated under a reduced pressure. A mixed solvent of ethanol and diethyl ether was added to the thus obtained residue, the insoluble matter was removed by filtration and then the filtrate was concentrated under a reduced pressure. The resulting residue was purified by silica gel column chromatography (eluent; n-hexane:ethyl acetate = 1:1 - 2:3) and then recrystallized from a mixed

solvent of ethyl acetate and n-hexane, thereby obtaining [4'-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]-1H-imidazole-4-carboxyanilide (35 mg) as colorless powder crystals.

Other compounds of Examples shown in the following Tables 2 and 3 were obtained in the same manner as described in the aforementioned Examples. Structural formulae and physicochemical properties of the compounds of reference examples are shown in the following Table 1, and structural formulae and physicochemical properties of the compounds of Examples are shown in Tables 2 and 3. In this connection, compounds having the chemical structures shown in Tables 4 and 5 can be produced easily in almost the same manner as the methods described in the aforementioned Examples or production methods, or by applying thereto slight modifications self-evident to those skilled in the art.

Abbreviations in the tables are Rex: Reference Example; Ex: Example; Co: compound number; Sy: production method (each numeral shows corresponding number of the aforementioned Example, indicating that the compound was produced by the same manner of the aforementioned Example); Str: structural formula; Dat: physicochemical properties (F: FAB-MS $(M + H)^+$; FN: FAB-MS $(M - H)^-$; E: EI-MS; M: melting point [°C]; (d): decomposition; N1: characteristic peak δ ppm of NMR (DMSO-$d_6$, TMS internal

standard); N2: characteristic peak δ ppm of NMR ($CDCl_3$, TMS internal standard); and *: absence of the group.

Table 1

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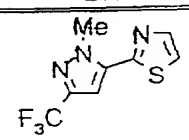
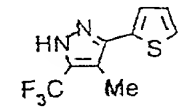
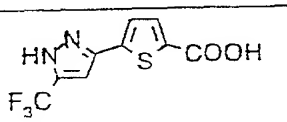
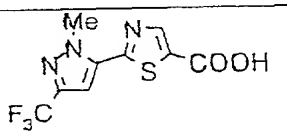
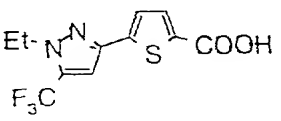
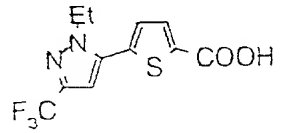
| 1 |  | N2: 4.32(3H,s), 6.90(1H, s), 7.45(1H, d, J=3.3Hz), 7.93(1H, d, J=3.0Hz) |
| 2 |  | N2: 2.29(3H, s), 7.16(1H, dd, J=5.2, 3.7Hz), 7.25(1H, dd, J=4.0, 1.0Hz), 7.44(1H, dd, J=5.4, 1.0Hz), 10.86(1H, brs) |
| 3 |  | N1: 7.07(1H,s), 7.60(1H,d,J=3.7Hz), 7.76(1H,d,J=3.7Hz), 14.42(1H,brs) |
| 4 |  | N1: 4.26(3H, s), 7.56(1H, s), 8.52(1H, s) |
| 5a) |  | N1: 1.42(3H,t,J=7.1Hz), 4.30(2H,q,J=7.2Hz), 7.46(1H,s), 7.58(1H,d,J=3.9Hz), 7.71(1H,d,J=3.6Hz), 13.18(1H,brs) |
| 5b) |  | N1: 1.39(3H,t,J=7.2Hz), 4.37(2H,q,J=7.2Hz), 7.15(1H,s), 7.53(1H,d,J=3.9Hz), 7.80(1H,d,J=3.9Hz), 13.46(1H,brs) |

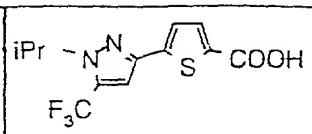
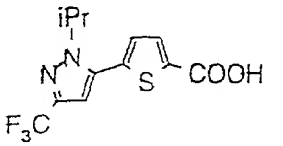
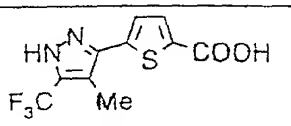
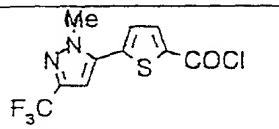
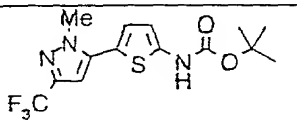
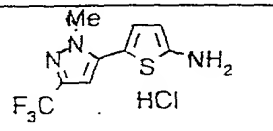
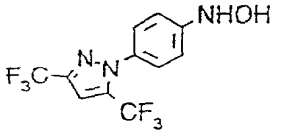
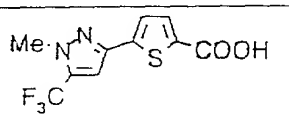
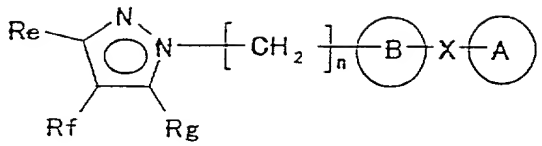
| | | |
|---|---|---|
| 6a) |  | N1: 1.49(6H,d,J=6.8Hz), 4.57-4.68(1H,m), 7.32(1H, s), 7.47(1H,d,J=3.9Hz), 7.50(1H,d,J=3.9Hz) |
| 6b) |  | N1: 1.44(6H,d,J=6.9Hz), 4.77-4.88(1H,m), 7.08(1H, s), 7.48(1H,d,J=3.9Hz), 7.80(1H,d,J=3.6Hz) |
| 7 |  | N1: 2.28(3H, s), 7.53(1H, d, J=3.9Hz), 7.81(1H, d, J=3.9Hz), 13.53(1H, brs), 14.11(1H, brs) |
| 8 |  | N2: 4.09(3H, s), 6.78(1H, s), 7.30(1H, d, J=4.4Hz), 8.00(1H, d, J=3.9Hz) |
| 9 |  | N2: 1.54-1.56(9H+$H_2O$,m), 4.00(3H, s), 6.50(1H, d, J=3.6Hz), 6.57(1H, s), 6.91(1H, d, J=3.9Hz) |
| 10 |  | N1: 3.96(3H, s), 6.29(1H, d, J=3.9Hz), 6.77(1H, s), 7.09(1H, d, J=3.9Hz), 7.1 (br) |
| 11 |  | F: 312 |
| 12 |  | F: 277 |

Table 2



( I a)

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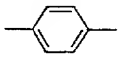
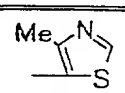
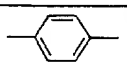
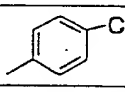
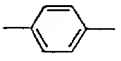
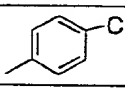
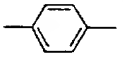
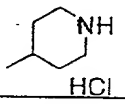
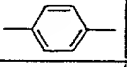
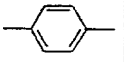
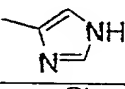
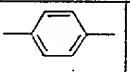
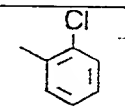
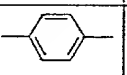
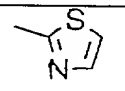
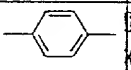
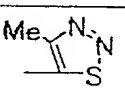
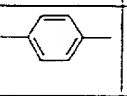
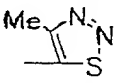
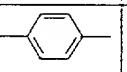
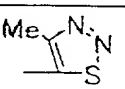
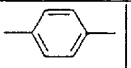
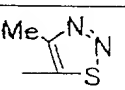
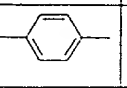
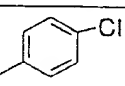
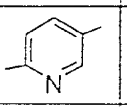
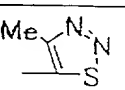
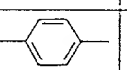
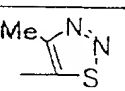
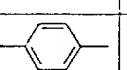
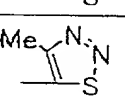
|---|---|---|---|---|---|---|---|---|---|
| 1 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | - | M:144-145 ; N1:2.64(3 H, s) |
| 2 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | - | M:196-197 ; N1:7.82(1 H, s) |
| 12 | H | COOH | $CF_3$ | 0 |  | NHCO |  | - | M:>300 |
| 13 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | - | F:407 |
| 14 | H | COOEt | $CF_3$ | 0 |  | $NHSO_2$ | Me | - | M:156-158 |
| 17 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | - | N1:10.23(1H, s) |
| 18 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:183-185 ; N1:7.82(1 H, s) |
| 19 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:174-175 ; N1:8.15(1 H, d, J=2.9Hz), 8.19(1 H, d, J=3.4Hz) |
| 20 | $CF_3$ | H | $CF_3$ | 0 |  | N(OH)-CO |  | 1 | M:126-129 ; N2:2.94(3 H, s), 7.10(1H, s) |
| 21 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:166-168 ; N1:2.84(3 H, s), 7.83(1H, s) |
| 22 | Me | H | Me | 0 |  | NHCO |  | 1 | M:101-103 |
| 23 | H | H | H | 0 |  | NHCO |  | 1 | M:184-186 |
| 24 | H | COOEt | $CF_3$ | 0 |  | NHCO |  | 8 | M:201-202 |
| 25 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:158-159 |
| 26 | H | COOEt | $CF_3$ | 0 |  | NHCO |  | 1 | M:118-120 |
| 27 | $CF_3$ | H | H | 0 |  | NHCO |  | 1 | M:158-161 |

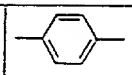
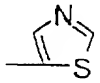
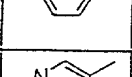
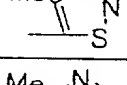
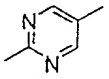
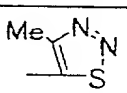
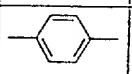
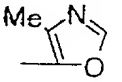
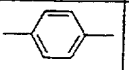
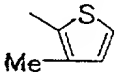
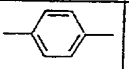
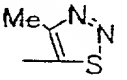
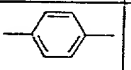
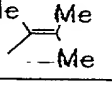
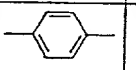
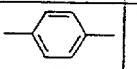
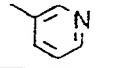
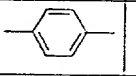
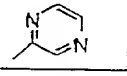
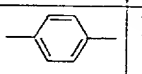
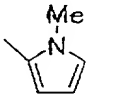
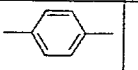
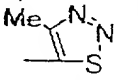
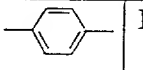
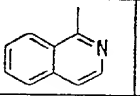
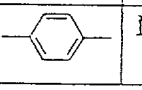
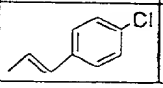
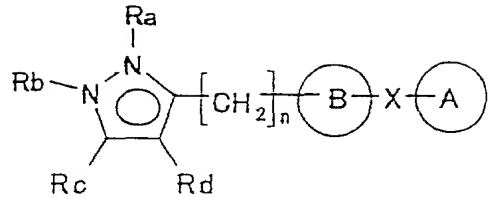
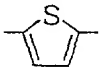
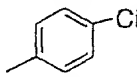
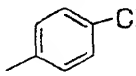
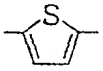
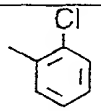
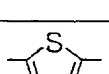
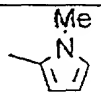
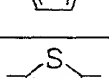
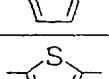
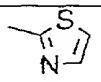
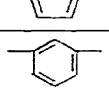
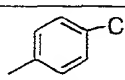
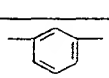
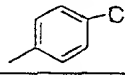
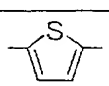
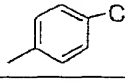
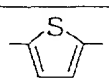
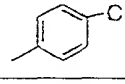
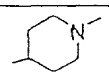
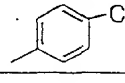
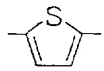
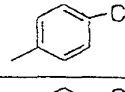
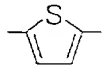
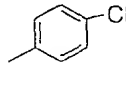
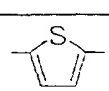
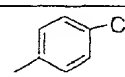
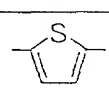
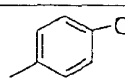
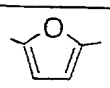
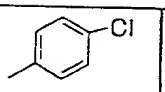
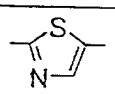
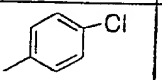
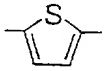
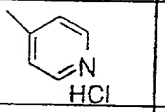
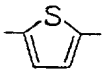
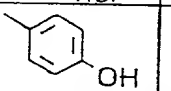
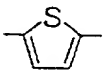
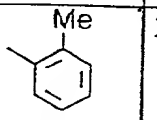
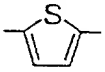
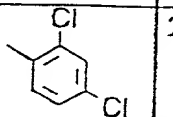
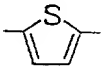
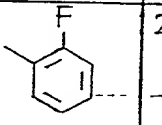
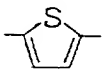
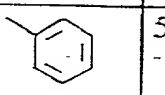
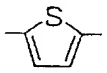
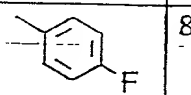
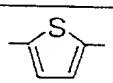
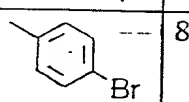
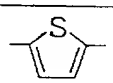
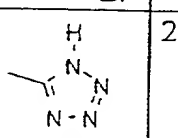
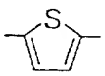
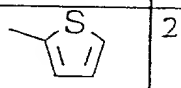
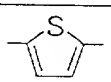
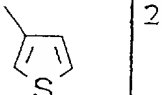
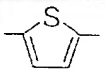
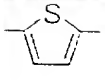
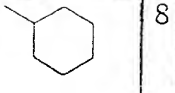
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 28 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:194-196 |
| 29 | H | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:133-135 |
| 30 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:215-218 |
| 31 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:135-136 |
| 32 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:169-172 ; N1:2.48(3H, s) |
| 33 | $CF_3$ | H | $CF_3$ | 1 |  | NHCO |  | 1 | M:125-126 |
| 34 | H | COOEt | $CF_3$ | 0 |  | NHCO |  | 1 | M:163-165 |
| 35 | H | COOEt | $CF_3$ | 0 |  | NHCO |  | 2 | M:141-143 |
| 36 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:188-190 ; N1:9.14(1H, d, J=1.5Hz) |
| 37 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:188-190 |
| 38 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:156 ; N1:3.90(3H, s) |
| 39 | $CF_3$ | H | $CF_3$ | 0 |  | CONH |  | 1 | F:422 |
| 40 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  | 1 | M:99-100 |
| 41 | H | COOEt | $CF_3$ | 0 |  | NHCO |  | 5 | M:176-178 |

Table 3



(I b)

| Ex | Ra | Rb | Rc | Rd | n | B | X | A | Sy | Dat |
|---|---|---|---|---|---|---|---|---|---|---|
| 3 | * | Me | $CF_3$ | Me | 0 |  | CONH |  | - | M:210-213 |
| 4 | Me | * | $CF_3$ | Me | 0 |  | CONH |  | - | M:192-196 ; N1:2.15(3H, s), 3.91(3H, s) |
| 5 | Me | * | $CF_3$ | H | 0 |  | CONH |  | - | M:156 ; N2: 4.08(3H, s), 7.13(1H, dt, J=7.8, 1.5Hz) |
| 6 | Me | * | $CF_3$ | H | 0 |  | CONH |  | - | M:158-159 ; N1:3.44(3H, s), 4.07(3H, s) |
| 7 | Me | * | $CF_3$ | H | 0 |  | CONH | Et | - | M:136-137 |
| 8 | * | Me | $CF_3$ | H | 0 |  | CONH |  | - | M:244-246 ; N2:4.04(3H, s) |
| 9 | * | Me | $CF_3$ | H | 0 |  | NHCO |  | - | M:173-175 ; N2:4.02(3H, s) |
| 10 | Me | * | $CF_3$ | H | 0 |  | NHCO |  | - | M:150-153 |
| 11 | * | Me | $CF_3$ | H | 0 |  | $CH_2NH$ |  | - | M:113-115 ; N2:4.48(2H, s) |
| 15 | Me | * | $CF_3$ | H | 0 |  | CH=CF (cis) |  | - | E:386 |
| 16 | Me | * | $CF_3$ | H | 0 |  | CONH |  | - | M:163-165 |
| 42 | * | H | $CF_3$ | H | 0 |  | CONH |  | 1 | M:246-247 |
| 43 | Et | * | $CF_3$ | H | 0 |  | CONH |  | 1 | M:177 ; N1: 1.51(3H, t,J=7.3Hz), 4.36(2H,q, J=7.3Hz) |
| 44 | * | iPr | $CF_3$ | H | 0 |  | CONH |  | 1 | M188-190 ; N1:4.59-4.70(1H, m) |
| 45 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 1 | M:204-206 ; N1:4.07(3H,s) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 46 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 1 | M:183-185 ; N2:4.13(3H,s), 6.78(1H,d,J=4.0 Hz) |
| 47 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 2 | M:163-164 |
| 48 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 8 | M:247(d) |
| 49 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 1 | M:185-186 ; N1:9.32(1H, s), 10.17(1H, s) |
| 50 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 2 | M:159-161 ; N2:4.06(3H, s) |
| 51 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 2 | M:181-183 ; N2:4.08(3H, s) |
| 52 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 2 | M:147-148 ; N1:4.08(3H, s) |
| 53 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 5 | M:129-130 ; N2:4.07(3H, s) |
| 54 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 8 | M:189-192 ; N2:4.07(3H, s) |
| 55 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 8 | M:191-192 ; N2:4.07(3H, s) |
| 56 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 2 | M:285-287(d) |
| 57 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 2 | N2:4.07(3H, s) |
| 58 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 2 | M:166-168 ; N2:7.13(1H, dd, J=4.9, 1.5Hz), 7.31(1H, dd, J=5.2, 3.2Hz), 7.68(1H, dd, J=3.0, 1.5Hz) |
| 59 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 5 | M:207-210 |
| 60 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 8 | M:140-141 ; N1:1.10-1.20(1H, m), 1.24-1.37(4H, m), 1.58-1.66(1H, m), 1.69-1.89(4H, m) |

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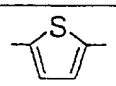
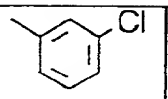
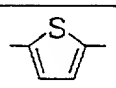
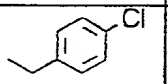
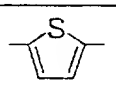
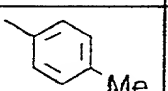
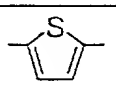
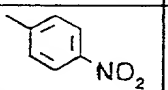
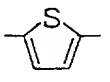
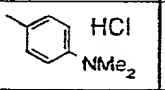
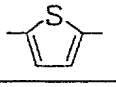
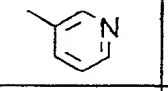
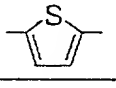
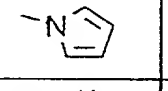
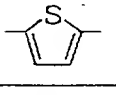
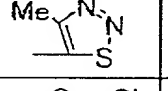
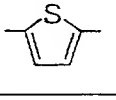
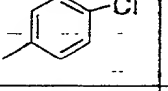
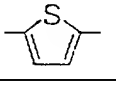
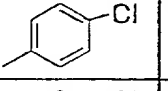
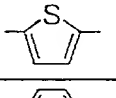
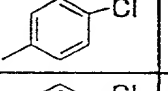
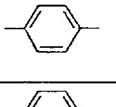
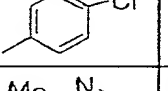
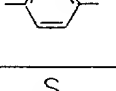
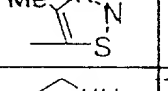
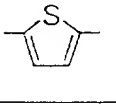
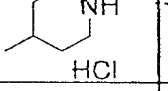
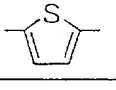
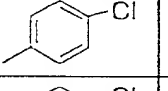
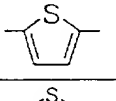
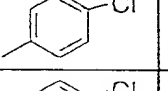
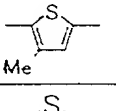
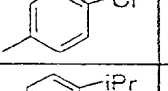
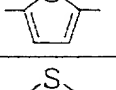
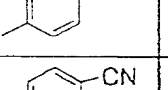
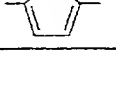
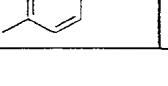
|---|---|---|---|---|---|---|---|---|---|---|
| 61 | * | Me | $CF_3$ | H | 0 |  | CONH |  | 1 | M:156-157 |
| 62 | * | Me | $CF_3$ | H | 0 |  | CONH |  | 1 | M:197-199 |
| 63 | * | Me | $CF_3$ | H | 0 |  | CONH |  | 5 | M:205-207 |
| 64 | * | Me | $CF_3$ | H | 0 |  | CONH |  | 5 | M:234-236 ; N2:4.04( 3H, m) |
| 65 | * | Me | $CF_3$ | H | 0 |  | CONH |  | 8 | M:230 |
| 66 | * | Me | $CF_3$ | H | 0 |  | CONH |  | 1 | M:195-196 |
| 67 | * | Me | $CF_3$ | H | 0 |  | CONH |  | 8 | M:211-215 |
| 68 | Me | * | $CF_3$ | H | 0 |  | NHCO |  | 1 | M:148-149 ; N1:2.86( 3H, s) |
| 69 | Me | * | $CF_3$ | H | 0 |  | CONMe |  | 5 | M:136-137 ; N1:3.35( 3H, s) |
| 70 | * | Me | $CF_3$ | H | 0 |  | NHCO |  | 8 | M:197-199 |
| 71 | Me | * | $CF_3$ | H | 0 |  | NHCO |  | 8 | M:166-168 ; N1:11.92 (1H, s) |
| 72 | Me | * | $CF_3$ | H | 0 |  | NHCO |  | 9 | M:187-188 ; N2:3.93( 3H, s) |
| 73 | Me | * | $CF_3$ | H | 0 |  | NHCO |  | 9 | F:368 ; N1:2.83(3H, s ) |
| 74 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 13 | M:265-266 |
| 75 | Me | * | Me | H | 0 |  | CONH |  | 1 | M:198-200 |
| 76 | Me | * | H | H | 0 |  | CONH |  | 1 | M:206-208 |
| 77 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 1 | M:162-164 |
| 78 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 8 | M:163-164 |
| 79 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 8 | M:211-214 |

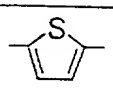
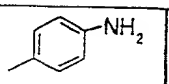
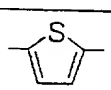
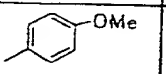
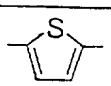
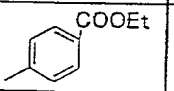
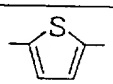
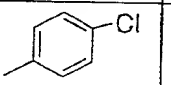
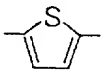
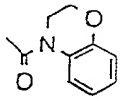
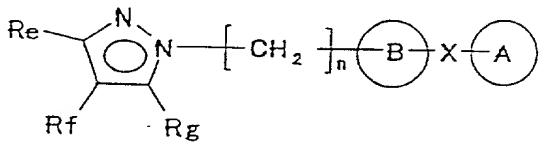
| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| 80 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 8 | M:181-183 |
| 81 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 5 | M:166-167 |
| 82 | Me | * | $CF_3$ | H | 0 |  | CONH |  | 5 | M:183-185 |
| 83 | Me | * | $CF_3$ | H | 1 |  | CONH |  | 1 | M:137-139 |
| 84 | Me | * | $CF_3$ | H | 0 |  |  | | 2 | M:153-155 |

Table 4



(I a)

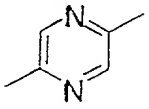
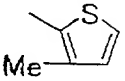
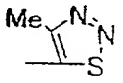
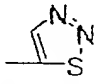
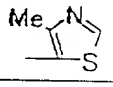
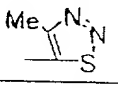
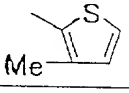
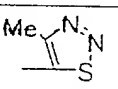
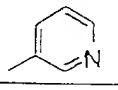
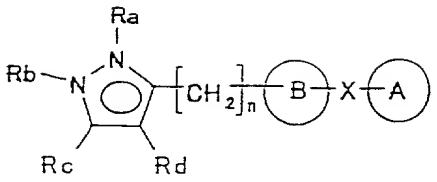
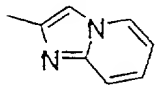
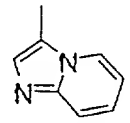
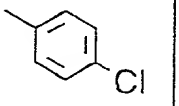
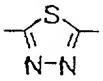
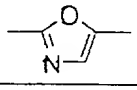
| Co | Re | Rf | Rg | n | B | X | A |
|---|---|---|---|---|---|---|---|
| 11 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  |
| 12 | $CF_3$ | H | $CF_3$ | 0 | | NHCO |  |
| 13 | $CF_3$ | H | $CF_3$ | 0 |  | NHCO |  |
| 14 | $CF_3$ | H | $CF_3$ | 0 | | NHCS |  |
| 15 | $CF_3$ | H | $CF_3$ | 0 | | NHCS |  |
| 16 | $CF_3$ | H | $CF_3$ | 0 | | NHCS |  |
| 17 | $CF_2CF_3$ | H | $CF_2CF_3$ | 0 | | NHCO |  |
| 18 | $CF_2CF_3$ | H | $CF_2CF_3$ | 0 | | NHCO |  |

Table 5



(I b)

| Co | Ra | Rb | Rc | Rd | n | | X | A |
|---|---|---|---|---|---|---|---|---|
| 1 | * | Me | $CF_3$ | H | 0 |  | CONH |  |
| 2 | Me | * | $CF_3$ | H | 0 | | CONH | |
| 3 | * | Me | $CF_3$ | H | 0 | | CONH |  |
| 4 | Me | * | $CF_3$ | H | 0 | | CONH | |
| 5 | * | Me | $CF_3$ | H | 0 | | CSNH |  |
| 6 | Me | * | $CF_3$ | H | 0 | | CSNH | |
| 7 | Me | * | $CF_2CF_3$ | H | 0 | | CONH | |
| 8 | * | Me | $CF_3$ | H | 0 |  | CONH | |
| 9 | Me | * | $CF_3$ | H | 0 | | CONH | |
| 10 | * | Me | $CF_3$ | H | 0 |  | CONH | |